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Diagnostics and the Challenge of Antimicrobial Resistance: a Survey of UK Livestock Veterinary Surgeons' Perceptions and Practices

Abstract

Background

This paper explores the current role and place of diagnostic tests in the treatment of farm animal disease. With the growing focus on reduced reliance on antibiotic medicines in both animal and human patient care, attention is increasingly being focused on the practice, the technology and the function of diagnostic tests and how these can support responsible antimicrobial use. Emerging diagnostic technologies offer the possibility of more rapid testing for bacterial disease, while food chain actors and others are increasingly seeking to make diagnostic tests mandatory before the use of critically important antibiotics.

Method

This paper reports the findings of a recent large-scale on-line survey of UK farm animal veterinary surgeons (N=135) which investigated current veterinary diagnostic practice with particular attention to the relationship between diagnostic test use and antibiotic treatment.

Results

Results revealed a range of factors that influence veterinary diagnostic practice and demonstrate the continuing importance of clinical observation and animal/herd knowledge in the selection of antibiotic treatment.

Conclusion

The findings identify a considerable ambivalence on the part of farm animal veterinarians regarding the current and future uses of rapid and point-of-care diagnostic tests as a means of improving clinical diagnosis and addressing inappropriate antibiotic medicine use.

INTRODUCTION

Reducing unnecessary and inappropriate use of antibiotics in farm animal production has become a key objective to combatting the emergence and transmission of antimicrobial resistance (AMR; BVA, 2015; RCVS, 2018; DEFRA, 2019). To date, attention has largely focused on two approaches. The first approach has been to contest particular rationales for using antibiotics in agriculture - whether these are to stimulate growth promotion (a use banned in the EU since 2006) or to prophylactically guard against the development and spread of endemic disease amongst herds and flocks. The second approach has been to reduce the prescription of particular classes of antibiotics, notably fluoroquinolones, higher order cephalosporins and colistin, considered critically important for human health (WHO, 2017; EMA, 2019). These strategies have already begun to achieve marked reductions in antibiotic use within veterinary medicine in the UK (RUMA, 2018; Veterinary Medicines Directorate, 2019). A third approach, which has arguably attracted less attention within the various policy and professional communities until recently, is one that focuses more specifically upon the processes, technologies and practices of veterinary diagnosis as a means to achieve responsible and more accurate antibiotic use. The Review on Antimicrobial Resistance, led by Jim O'Neill, identified the need for better diagnostic tests 'to ensure better-targeted and more appropriate veterinary prescribing' (O'Neill, 2016a), arguing that more rapid tests would allow farmers and veterinarians to intervene in a more timely manner to identify bacterial infection and to prevent disease spread. Others too have identified rapid and point-of-care diagnostic tests as a means to confirm primary disease agents and enable appropriate treatment decisions (Anfossi et al., 2018; JAPIAMR, 2018). The European Commission Guidelines for the prudent use of antibiotics in veterinary medicine (2015/C 299/04, p.23) strongly recommends the use of rapid diagnostic tests as an effective way to reduce antibiotic use in farm animal production. Most recently, in a significant shift to market-driven forms of regulation, the UK's Red Tractor assurance and certification scheme now requires veterinarians on participant farms to only use Highest Priority Critically Important Antimicrobials (HPCIAs) as a last resort and only when supported by sensitivity testing and/or diagnostic testing (Red Tractor 2018). However, while there has been significant recent growth in research exploring the development of rapid diagnostics in human medicine (for example to test for toxicology, sensitivity and cardiometabolic and infectious diseases: (Di

Ruffano et al., 2012; Kaman et al, 2013; Ndibuagu et al., 2017; Wojciechowski, 2017), there is relatively little empirical research looking at the role of rapid tests, and diagnostic practices in general, within contemporary veterinary decision-making in achieving responsible antibiotic use (Griffioen et al., 2016). The aim of the current study was therefore to investigate current diagnostic practices amongst UK veterinary surgeons and the opportunities and barriers that might exist for new and current rapid and point-of-care tests to contribute to reducing antibiotic use on farms.

Materials and methods

Participants

An online questionnaire was developed in autumn 2018 and made available to all livestock veterinarians with membership of the British Veterinary Association (BVA) in November/December 2018. A draft online version of the survey was initially piloted and tested using selected veterinarians from the cattle, pig and poultry sectors (16 veterinarians) and academic veterinarians from a veterinary school (4 veterinarians). The questionnaire was then refined, formatted and made available to the target population using Qualtrics software interface (Qualtrics, Provo). Before data collection, ethical approval was granted by the University of Exeter Geography Ethics Committee (approval reference number eCLESGeo000069v.3.0). Respondents' participation was voluntary and anonymous. The online questionnaire was also advertised on social media (e.g. Twitter) and within the *Veterinary Record*. When the questionnaire was closed, 190 veterinarians had responded.

Questionnaire structure

The questionnaire has been included as supplementary material (Appendix 1). It had four sections and was comprised of 25 questions in total. The first section asked for participant demographics, followed by a series of questions on current use of diagnostic tests. This section included an open question for respondents to list the six diagnostic tests they used most often (examples were provided to help respondents answer this question). The answers to this question led to a follow-up question asking where these tests were done (on the farm, in a practice lab, etc.). A third section explored participants' experience and possible future

use of pen-side or point-of-care tests and the questionnaire closed with a set of questions on the relationship between diagnostic procedures and antibiotic prescription and use. A five-point Likert-type scale with the options 'Always (>75% of the time)', 'Often (50-75%)', 'Sometimes (25-50%)' 'Rarely (<25%)' and 'Never (0%)' was used to categorise frequencies and respondents' decisions to undertake a diagnostic test (Figure 1). A similar five-point scale was also used to evaluate the degree of agreement to statements regarding the use of rapid diagnostic tests with responses ranging from 'strongly agree' to 'strongly disagree'.

Data entry, management and analysis

Data imported from the Qualtrics software were initially processed through MS Excel (Microsoft, Redmond) and collated into a form suitable for descriptive analysis. Subsequent data cleaning reduced the number of fully usable responses to 153 (largely following the removal of partially answered questionnaires). Some individual questions remained unanswered in the retained questionnaire returns, meaning that the number of responses per question was at times less than the total number of respondents. Qualitative text analysis, following an inductive coding method (Maquire and Delahunt, 2017), was used to categorise and compare open-ended questions regarding the principal bacterial diseases identified by respondents and the relevant diagnostic test procedures employed. The results are presented here in a variety of forms; following quantitative and qualitative analysis and through direct quotations from open-ended returns.

Results

General Respondent Information

Of the respondents to the survey, 54% identified as female and 42% identified as male veterinarians. The largest group of respondents (27%) graduated between 2014 and 2018 with a further 17% graduating between 2009 and 2013. In total, almost half of respondents graduated within the last 10 years. In terms of their work environment, more than half of respondents (53%) worked in practices of between 1 and 5 full-time veterinarians; the remainder worked in practices of variable but larger size. Geographically, a large number of respondents were from the South West of England (26%) and Wales (19%), possibly reflecting areas of high livestock and farm density.

The largest single group of respondents (37%) worked for independent veterinary practices, while 20% worked for corporate veterinary practices. The remainder were either self-employed (15%) or had a range of different occupations including government veterinarians, academic veterinary scientists and consultants, pharmaceutical company and zoo veterinarians, retired veterinarians and Scottish Veterinary Investigation Officers.

The bulk of respondents referred to themselves in generic terms as 'farm vets' or 'mixed practice vets' (Table 1), though well over half (63%) of these spent the majority of their working time with cattle (dairy of beef). Few of the respondents identified themselves specifically as pig or poultry veterinarians (Table 1). As the last available RCVS survey of the veterinary profession (Robinson et al., 2014) has shown, pig and poultry work is today a relatively minor component of current veterinary working time.

Although evidence suggests that the proportion of overall veterinary input to farms has decreased in recent years (Robinson et al. 2014), responses to this survey showed that on-farm work, whether routine (including checking fertility, performing castrations, dehorning, blood sampling and monitoring the health of farm animals), preventative (preventative medicine and treatment; herd, flock or group health planning advisory services and consultancy) or reactive (emergency services and therapeutic treatment), accounted for an estimated two thirds of respondents' professional workload.

Table 1: 'How Would You Describe Your Veterinary Work?'

Descriptions of veterinary role	***No of vets and %***
A cattle vet	36 (25%)
A pig vet	5 (3%)
A poultry vet	8 (5%)
A farm vet	44 (30%)
A mixed practice vet	36 (25%)
Other [1]	17 (12%)

[1] **'**Other' included animal scientists and aquaculture consultants, veterinary nutritionists, veterinary investigation officers, pathologists, small ruminant veterinarians, sheep veterinarians, veterinarians working for the Veterinary Medicines Directorate, game bird veterinarians, a government veterinarian, and companion animal and equine veterinarians.

Diagnostic Testing

Survey results revealed that, most of the time, veterinarians prescribe antibiotics without a specific diagnostic test (whether undertaken on-site or in a laboratory). The majority of respondents (70%) reported prescribing most antibiotic treatments over the last year without undertaking a diagnostic test. To understand the circumstances when a test would and would not be used for a variety of conditions (including both those that are relevant to and those that have little relation to antibiotic use), respondents were asked to estimate the relative frequency with which certain factors were taken into account in their decision to undertake a diagnostic test when confronted with the possibility of animal illness (Figure 1).

Insert Figure 1 in or near here

Clearly certain considerations, such as the need to conform to statutory requirements and the monetary value of the animal/flock, are frequent (and in some cases, mandatory) components in the decision to undertake a diagnostic test. Conversely, the sentimental value of the animal, unfamiliarity with the species and the specific demands of the client are rarely if ever considered as valid reasons to run a diagnostic test. More interesting, and to some extent expected, are the variations in the relative importance of diagnostic tests in, on the one hand, exploring unexplained change in animal health and, on the other hand, confirming the presence of a suspected infection. That 35% of respondents 'always' used tests to confirm a diagnosis, while only 14% 'always' used tests as a means to account for unexplained changes suggests that diagnostic tests are predominantly used as a 'rule in' mechanism and much less as a 'rule out' mechanism.

The need, or the requirement, to monitor for endemic or subclinical disease presence is also revealed as a common consideration with 52% of respondents claiming this is 'always' or 'often' a factor in their use of diagnostic tests. Current widely-practiced veterinary testing and monitoring regimes for endemic or subclinical diseases such as Bovine Tuberculosis (bTB), Johne's disease and Bovine Viral Diarrhoea (BVD) undoubtedly account for a significant proportion of these considerations. To explore this in greater depth, veterinary surgeons were asked to identify the diagnostic tests they used most frequently. Amalgamating the responses into four 'target' categories (Table 2), tests were almost equally divided between

those undertaken to rule-in (confirm) or rule-out (exclude) a specific or named infectious agent (such as Tuberculosis or Johne's disease) and those carried out in response to a broader clinical indication (such as mastitis, lameness due to infection causes, scour or respiratory disease). To monitor the health status of farm animals, veterinarians also recorded undertaking tests in response to observed nutritional and metabolic states including hypocalcaemia and ketosis. In certain cases, respondents also employed diagnostic tests for antibiotic residues.

Table 2: Categories of diagnostic tests undertaken most frequently by respondent UK veterinarians over the last 12 months up to survey date (N=136): Authors' survey, 2018/19.

Test target	Sub-categories	Examples
Infectious agent	Bacterial	Tuberculosis, Johne's disease, Salmonella, Brucella, non-specified bacterial infection
	Viral	Bluetongue, Gumboro, Porcine Reproductive and Respiratory Disease, Bovine Viral Diarrhoea
	Parasitic/protozoal	Neospora, endoparasitic infections
Clinical indication	Mastitis Lameness Diarrhoea (scours) Respiratory disease Failure of passive transfer	Milk constituents, somatic cell count, Infectious causes
Physiological state	Nutritional/Metabolic state/Breeding Soundness	Hypocalcaemia/hypomagnesaemia, ketosis, non-esterified fatty acids, rumen fill, trace element levels, body condition score
Other	Antibiotic residues	

Note: The free-text responses which described the diagnostic tests that the respondents used most frequently were coded by three authors who are also veterinarians, with the aim of identifying the diagnostic targets of the rapid tests as perceived by the respondents. The responses included both clinical indications for performing a test, and infectious agents as test targets. Some degree of overlap is therefore inevitable. However, the responses provide valuable insight into the most common clinical indications and infectious agents that trigger diagnostic testing.

In looking at the specific characteristics of different diagnostic tests that are valued by veterinarians (Figure 2), three key qualities emerge: reliability and accuracy of the test (58% indicating 'very important'); cost (35% indicating 'very important'); and the waiting time (21% indicating 'very important'). Reputation, positive test experience, equipment availability and ease of use were also important (>50% 'important' or 'very important'). Respondents were

not as likely to associate frequency of use or peer recommendation as important (<50% 'important' or 'very important').

Insert Figure 2 in or near here

Using rapid and point-of-care diagnostic tests

Rapid and point-of-care diagnostic tests [2] are not a universal feature of contemporary farm animal veterinary practice. Respondents to this survey were fairly evenly divided between those that did not use these types of diagnostic tests or used them rarely (42%) and those used these types of diagnostic tests sometimes or often (58%). For the latter, their value lay chiefly in the speed with which treatment decisions could not only be confirmed but also, and crucially, which could be justified and defended to the farmer. The ability to show a farmer on-site that, for example, antibiotics were unnecessary following a rapid test result was identified by a number of respondents (54%) as a distinct value of rapid tests. Rapid tests allow veterinarians to '*show the test results for their farmers and help [them] understand not all disease is bacteria*' (Respondent S049 [3], 2019), thereby strengthening the veterinarian's justifications for prescribing or not prescribing. Veterinarians who did not use rapid and point-of-care tests preferred to either trust their clinical experience and observational skills or to employ more conventional laboratory routes. As one respondent felt, '*We have plenty of scope to make better decisions based on clinical observation. We over-estimate the potential to accurately prescribe based on test results*' (Respondent S031, 2019).

Respondents were asked to indicate their level of agreement with a series of statements regarding the use of rapid diagnostic tests (Figure 3). There was a high proportion of 'disagree' responses (62%) to the statement that veterinarians 'need more rapid diagnostic tests for the diseases they commonly encounter'. However, 61% of respondents agree that there is a 'need for more on-farm tests' as current lab-based tests are time-consuming. According to one respondent (Respondent S015, 2019): '*It takes too long to wait for a culture and sensitivity*

[2] The questionnaire intentionally left 'rapid' and 'point-of-care' diagnostics undefined so as to enable a range of interpretations from respondent veterinarians. In this study, 'rapid' or 'point-of-care' diagnostics would be those that provide a result while the veterinarian is still on the farm with the animal tested.

[3] Respondents were numbered according to date of submitted response.

report from a laboratory … farmers want an instant decision when discussing treatments for a sick animal.'

Critically, as stated by one respondent, future rapid diagnostics could help to '*differentiate viral and bacterial causes of animal diseases such as pneumonia*' (Respondent S110, 2019). Yet this interest was also accompanied by concern over certain practicalities of current rapid diagnostic tests. The survey revealed a similar degree of ambivalence over the reliability of rapid tests with 38% of respondents neither agreeing nor disagreeing with the statement that 'there are difficulties to interpret the results with on-farm tests'. Current rapid diagnostic tests, according to one respondent, frequently '*lack information on sensitivity and specificity for the veterinarian*' (Respondent S018, 2019) while, for another: '*It could be useful as one more bit of information for the interpretation of the clinical case, when used by the veterinarian, in the decision making for the use of antibiotics and for which antibiotics to use'* (Respondent S069, 2019).

Insert Figure 3 in or near here

The equivocal nature of these responses suggests that opinion is relatively divided on the current and future use of rapid, on-farm and point-of-care tests. The open-ended responses hint at differences across production sectors, though the numbers involved are too small to achieve statistical significance. Nevertheless, some veterinarians were more in favour of rapid tests because they were seen as providing a valid addition to the repertoire of diagnostics within the cattle sector, while others noted that rapid diagnostic tests were not '*readily available and economically viable to conduct bacteria tests on pig and poultry sectors*' (Respondent S124, 2019). Finally, when asked to identify any bacterial diseases and farm animal infections for which 'new, good and reliable diagnostic tests were still needed', veterinarians prioritised (in terms of numbers of times mentioned) the following: bTB (21 respondents), Johne's disease (16 responses), mastitis (13 respondents), pneumonia (12 respondents), *Mycoplasma*-related diseases (10 respondents) and salmonella (7 respondents). Less frequently mentioned, reflecting the distribution of veterinary specialisms captured in the survey as mentioned above, but nonetheless useful to note here, were ileitis and swine dysentery in pigs and *E. coli* in poultry.

Diagnosis and antibiotic treatment decision making

Veterinarians were asked to consider the relationship between diagnostic testing and antibiotic prescription. Diagnostic tests were not generally used to confirm the prior choice of an antibiotic treatment once it had been prescribed (38% claimed this was never the case over the last year and a further 36% stated this happened in only a few cases). Moreover, few veterinarians routinely undertook a susceptibility test before an antibiotic treatment decision (57% responded 'rarely' and 28% 'never').

Although survey responses displayed considerable variation with respect to the use and relative advantages (or disadvantages) of pen-side and point-of-care diagnostic tests, responses were notably more unified in their agreement with the statement that more readily available rapid diagnostic tests would help in achieving more sustainable use of antibiotics: 92% of respondents selected 'yes' or 'sometimes'. As stated by one respondent: '*If we can prove the disease on farm by using rapid diagnostics, we can pinpoint the best antimicrobial at that time and save waiting for failure treatment*' (Respondent S028, 2019).

Finally, veterinarians were asked, 'When treating the farmed species with which you work the most, what proportion of antibiotic treatment courses were prescribed over the last 12 months for the following reasons: to treat sick animals, to prevent the spread of disease or to reduce the likelihood of disease.' The most common use of antibiotics was for Option 1, the treatment of sick animals (74% answering 'most' or 'all' treatment courses). Options 2 and 3 were rarely cited as a reason for antibiotic use; 52% indicated they had never used antibiotic treatments to reduce the likelihood of a disease occurring or developing over the last 12-month period, whilst (8%) indicated they had never used antibiotics to prevent the spread of a disease already present in the flock or herd.

DISCUSSION

Current arguments around achieving more sustainable antibiotic use in both humans and animals frequently point to the need to reduce unnecessary or inappropriate treatment. For many (Anomaly, 2019; Down et al., 2017; Krömker and Leimbach, 2017; O'Neill, 2016a, 2016b), a key mechanism for achieving this is better and faster diagnostic tests, not only to

ensure that the medicines deployed are appropriately targeted to bacterial pathogens but also to justify decisions to employ those medicines, particularly in cases where critically important antibiotics are deemed necessary to protect animal or herd/flock health. In the light of such arguments, the present study sought to identify current approaches amongst farm animal veterinarians to both diagnostic tests generally as well as rapid and point-of-care tests in particular in the context of their relationship to antibiotic use. Three key points emerged from the survey.

Firstly, for many of the more commonly encountered farm animal diseases or infections, specific diagnostic tests were not considered necessary nor are they regularly used, even when the subsequent treatment involves antibiotics. Most veterinarians appeared confident in their clinical observation and expertise, often drawing upon previous pathologies or prior test results within known herds and flocks to make subsequent treatment decisions (Owens et al. 1997; Eriksen et al, 2019). Certain endemic and production diseases are common, and tests, when used, are generally there to confirm (rather than exclude) a diagnosis. Such confirmation can be useful to the veterinarian not only in justifying subsequent treatment costs to the farmer but also as a basis for encouraging the implementation of animal management measures to reduce the spread or occurrence of infection.

Secondly, the survey revealed a number of mixed, and, in places, contradictory, approaches to the use and future development of pen-side and point-of-care diagnostic tests. Respondents would like to see more rapid and point-of-care tests made available to shorten the time between test result and treatment (as previously described by Griffioen et al., 2016) to confirm particular diseases such as mastitis, and to easily differentiate between bacterial and non-bacterial infections. Many felt strongly that rapid tests have a place in achieving more sustainable use of antibiotics, but few used them regularly**.** Many also acknowledged concerns regarding their sensitivity, specificity and ease-of-use. At the time of this study, veterinary practitioners in the cohort surveyed did not view rapid and point-of-care diagnostic tests as a panacea for the unnecessary use of antibiotics in veterinary treatment.

Thirdly, the study underlined the complexity of disease diagnosis and treatment within the context of livestock farming where different bacterial pathogens can be present in an animal

without causing clinical disease until a precipitating factor - such as stress or a viral infection - occurs. These multiplicities can make diagnostic testing - and particularly a reliance on more simplistic pen-side and point-of-care devices - problematic. As one respondent pig veterinarian put it in an open-ended question: '*In pig medicine, it is not diagnostics but complexity of infectious diseases which make decisions on antibiotic choice challenging'* (Respondent S081, 2019). As others have shown and veterinarians may know, treatment decisions do not necessarily follow the outcomes of the bacteriological culture and susceptibility tests (Krömker and Leimbach, 2017; Jensen et al., 2017).

This exploratory study offers a valuable and original multidisciplinary investigation of veterinary diagnostic practice and the use of diagnostic tests in farm animal veterinary medicine. There is relatively little literature on veterinary diagnostic practice, yet current interest in the more sustainable use of antibiotic medicines seems to be resulting in particular emphasis on how diseases are identified in field situations and upon the treatment decisions that follow. The principal limitation of the study lies in the overall balance of the responses. Although 190 farm animal veterinarians from across the UK responded to the survey, it is difficult to precisely determine what proportion of currently practising farm animal veterinarians this represents, as accurate figures on this population are notoriously difficult to establish. However, as a figure, 190 responses is comparable to other recent surveys of farm animal veterinarians (Ison and Rutherford, 2014; Scherpenzeel et al., 2018) and although the number of self-identified pig and poultry veterinarians was relatively small compared to cattle veterinarians, their number is consistent with estimates of the proportion of time spent on these species within the veterinary profession (Robinson et al., 2014). Responses to this survey indicated that those describing themselves as 'farm' or 'mixed practice' veterinarians covered a suitable range of species and experiences.

Limitations

This online survey used a sampling frame of BVA members and others who engaged through social media. The study population represented only a small proportion of the veterinary profession of the UK despite collaboration with a national and well-subscribed body along with efforts to recruit respondents as widely as possible. Geographical bias is also likely to

have occurred due to overrepresentation of cattle veterinarians, many of whom are located in South West England. Early career veterinary surgeons were also over-represented, which might have added to responses about unfamiliarity with diagnostic tests. To address these limitations, further studies are being conducted to offer triangulation with this survey data through in-depth interviews with veterinarians at different levels of seniority and geographical spread.

CONCLUSION

This exploratory study offers insights into veterinarians' attitudes and approaches to diagnostic procedures and the use of diagnostic tests in the treatment of farm animal illness and disease within the context of growing societal and professional concern over the use of antibiotics in farm animal veterinary medicine. The study shows that diagnostic tests are far from universally used in determining disease, with many farm animal veterinarians preferring to rely on their own observational and clinical skills and experience in making treatment decisions. This is specifically shown to be the case for treatments involving antibiotics. Moreover, where antibiotics are used, it is generally for therapeutic treatment rather than prophylaxis or metaphylaxis. Finally, this study reveals a varied set of attitudes and approaches to the use of point-of care tests and identifies generalised patterns of using rapid diagnostic technologies across cattle, pig and poultry sectors in the UK. Despite the potential for rapid diagnostics to support sustainable antibiotic use in livestock - as identified in the O'Neill report - the results presented indicate that this is not standard practice at present. What is not clear is to what extent lack of use is caused by a lack of available technology or by limited uptake of novel tests by veterinary surgeons. This baseline information is currently being used to design a series of in-depth interviews with farm animal veterinarians to better understand their practical experiences, choices and other social and economic factors relating to the use of rapid diagnostics as well as their contribution to the management of animal health and reduction of inappropriate antibiotic use.

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